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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/416,267	10/12/1999	KUI SU	PF270P1	5938

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EXAMINER	
MERTZ, PREMA MARIA	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/416,267	Applicant(s) Su et al.
	Examiner Prema Mertz	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Sep 4, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *25-79* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *25-79* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☒ Interview Summary (PTO-413) Paper No(s). *16*
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Prosecution on the merits of this application is reopened on claims 25-79 considered unpatentable for the reasons indicated below:

Claim rejections-35 U.S.C. § 101

2. Claims 25-79 are rejected under 35 U.S.C. 101.

This rejection is maintained for reasons of record set forth at pages 3-5 of the previous Office action (Paper No. 10, 9/7/00) and pages 2-6 of the previous Office action (Paper No. 13, 5/8/01) .

Applicants argue that the burden is on the Examiner to establish why it is more likely than not that one of ordinary skill in the art would doubt the statement of utility, and that the specification on page 3, lines 5-8, teaches that the polypeptide of the present invention may stimulate cell proliferation and/or differentiation and may be used to treat, for example, restenosis and/or inflammation. Applicants have also asserted that the polypeptides of the instant invention have further related uses, for example in the detection of neoplasia. Applicants have submitted the Graf et al and Oelgeschlager et al references which teach that the polypeptide of the instant invention shares 100% identity with the human homologue of the twisted gastrulation protein from the fruit fly and Xenopus, respectively, which protein directly interacts with BMPs and that this polypeptide functions by a similar mechanism in vertebrates and flies. However, contrary to Applicants arguments, Applicants assertion of utility is not specific because one of ordinary skill in the art would not conclude that the claimed protein would be expected to have the same biological function in fruit flies, amphibians and humans. Furthermore, Applicants assertion (page 3, lines 5-8) that the instant protein may be involved in restenosis (defined as recurrence of stenosis after corrective surgery on the heart valve) and

inflammation (defined as a pathologic process consisting of a dynamic complex of cytologic and histologic reactions that occur in the affected blood vessels and adjacent tissues in response to an injury or abnormal situation caused by a physical, chemical or biologic agent), are unsupported by the disclosure of Oelgeschlager et al in which discloses the involvement of the claimed protein in central nervous system development. Therefore, Applicants assertion that the instant protein can be employed to treat, for example, restenosis and/or inflammation is not a credible, substantial or specific utility. To grant Applicant a patent on the assertion that the claimed polypeptide may stimulate cell proliferation and/or differentiation, is clearly prohibited by this judicial precedent since the compensation to the public is not commensurate with the monopoly granted.

Applicants argue that the claimed polypeptide has a specific and substantial utility because it can be used in detection of neoplasia. However, contrary to applicants arguments, the instant protein has no demonstrated function. The employment of the claimed polypeptide in such a method is not a substantial or specific utility, because the instant polypeptide has not been shown to be associated with neoplasia and there is no evidence on the record that it is associated with neoplasia. Such utilities are analogous to the assertion that a particular DNA can be employed as a molecular weight marker, which is neither a specific or substantial utility.

Appellants further argue the utility of the claimed polypeptide in the diagnosis of diseases of the immune system. However, in order for a polypeptide to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the polypeptide itself and a disease or disorder. If a molecule is to be used as a marker for a disease state, some disease state must be identified in some way with the molecule. There must be some expression

pattern that would allow the claimed polypeptide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the polypeptide is either present only in neoplastic tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. over expression). Evidence of a differential expression might serve as a basis for use of the claimed polypeptide as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed protein and any disease or disorder and the lack of any correlation between the claimed protein with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

A protein of unknown function would have utility if it can be employed as an indicator of a diseased state or of the presence of a disorder. The only disclosed function for a protein of the instant invention in the application as filed, however, is as a human cytokine protein akin to the TSG gene found in Drosophila which protein, may be employed for preventing, ameliorating, or correcting dysfunctions or disease or augmenting actions of such genes (page 2, lines 5-10). It is certain that this protein can be employed to identify compounds which can act as agonists or antagonists of the protein (page 4, lines 14-29; page 5, lines 1-5), but this information is without real value because the instant specification does not identify a physiological process such as blood pressure, heart rate, taste, cognition, or sensation of pain which one could expect to influence by the administration of a

compound that has been identified by employing a protein of the instant invention. If a protein of the instant invention bound to a compound of any appreciable value then the protein would have utility in the purification of that compound, but the instant specification, as filed, does not identify any specific compound which is known to bind to that protein. Applicant is not being required to identify a specific compound that binds to the instant protein, **and** a physiological process mediated thereby **and** a disease or disorder for which that protein is a marker. Applicant is only required to identify **one** substantial, specific and credible utility and, as stated in the previous office action, the employment of this protein only as the subject of further research does not satisfy the utility requirement of 35 U.S.C. § 101 because the courts have interpreted this statute as requiring an invention to have "substantial utility" "where specific benefit exists in currently available form".

An application has to be complete as filed, it is not a starting point of further research. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicants claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966)*, in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the Court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The Court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The protein encoded thereby are compounds which are known to be structurally analogous to (35.922% identity in the first 221 amino acid residues) the twisted gastrulation gene (TSG) in Drosophila (page 14, lines 25-28). In the absence of a knowledge of the biological significance of this protein in the instant specification as filed, there is no immediately obvious "patentable" use for it.

Each clinical agent which has been developed by measuring its interaction with a specific protein was evaluated against a protein whose physiological function was known. More importantly, an artisan knew, before they employed a specific protein to identify clinically useful compounds, which physiological process or processes they wished to manipulate and that the protein employed in their assay had an influence of that process. Even if one identifies an agonist or antagonist for a protein of the instant invention, this information is useless since one has no idea of what clinical effect the administration of that agonist or antagonist to an individual would have.

The following is an excerpt from M.P.E.P. 2138.05:

"CLAIMED INVENTION IS NOT ACTUALLY REDUCED TO PRACTICE UNLESS THERE IS A KNOWN UTILITY

Utility for the invention must be known at the time of the reduction to practice. Wiesner v. Weigert , 212 USPQ 721, 726 (CCPA 1981) (except for plant and design inventions); Azar v. Burns , 188 USPQ 601, 604 (Bd. Pat. Inter. 1975) (a composition and a method cannot be actually reduced to practice unless the composition and the product produced by the method have a practical utility); Ciric v. Flanigen , 185 USPQ 103, 105 - 6 (CCPA 1975) ("when a count does not recite any particular utility, evidence establishing a substantial utility for any purpose is sufficient to prove a reduction to practice"; "the demonstrated similarity of ion exchange and adsorptive properties between the newly discovered zeolites and known crystalline zeolites ... have established utility for the zeolites of the count"); Engelhardt

v. Judd , 151 USPQ 732, 735 (CCPA 1966) (When considering an actual reduction to practice as a bar to patentability for claims to compounds, it is sufficient to successfully demonstrate utility of the compounds in animals for somewhat different pharmaceutical purposes than those asserted in the specification for humans.); Rey - Bellet v. Engelhardt,181 USPQ 453, 455 (CCPA 1974) (Two categories of tests on laboratory animals have been considered adequate to show utility and reduction to practice: first, tests carried out to prove utility in humans where there is a satisfactory correlation between humans and animals, and second, tests carried out to prove utility for treating animals.).

A PROBABLE UTILITY MAY NOT BE SUFFICIENT TO ESTABLISH UTILITY

A probable utility does not establish a practical utility, which is established by actual testing or where the utility can be "foretold with certainty." Bindra v. Kelly , 206 USPQ 570, 575 (Bd. Pat. Inter. 1979) (Reduction to practice was not established for an intermediate useful in the preparation of a second intermediate with a known utility in the preparation of a pharmaceutical. The record established there was a high degree of probability of a successful preparation because one skilled in the art may have been motivated, in the sense of 35 U.S.C. 103, to prepare the second intermediate from the first inter mediate. However, a strong probability of utility is not sufficient to establish practical utility.); Wu v. Jucker , 167 USPQ 467, 472 (Bd. Pat. Inter. 1968) (screening test where there was an indication of possible utility is insufficient to establish practical utility). But see Nelson v. Bowler , 206 USPQ 881, 885 (CCPA 1980) (Relevant evidence is judged as a whole for its persuasiveness in linking observed properties to suggested uses. Reasonable correlation between the two is sufficient for an actual reduction to practice.)."

Therefore Applicants have failed to establish a practical utility for a protein of the instant invention at the time the application was filed.

In conclusion, Applicants arguments with respect to utility of the instant polypeptide, are found to be non-persuasive. Contrary to Applicants arguments, the instant specification does not disclose a single credible, specific or substantial utility for the instant polypeptide. The initial burden to demonstrate or present such is on Applicants.

Claims 25-79 also remain rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the

reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (703) 308-4229. The examiner can normally be reached on Monday-Friday from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Prema Mertz

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
September 13, 2002